Author’s response to reviews

Title: Spoligotyping based genetic diversity of Mycobacterium tuberculosis in Ethiopia: A systematic review

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Point by point response:

1. Introduction section:

• Page 2, second paragraph, final sentence: “In Ethiopia, according to the recent national TB drug resistance surveillance report, 2.3% of new TB cases and 17.8% of previously treated TB cases were estimated to have MDR,” rephrased as: “In Ethiopia, based on the latest national anti-TB drug susceptibility surveillance report, a significantly higher proportion of MDR TB cases were reported among previously treated cases (17.8%) compared to newly diagnosed TB cases (2.3%).”

• Page 3, paragraph 5, under Genomics of M. tuberculosis sub section: the whole paragraph is paraphrased as: “Human TB is predominantly caused by M. tuberculosis which is a member of M. tuberculosis complex (MTBC) know by identical 16S rRNA sequences and 99.9% similarity at nucleotide level. Briefly, the members of MTBC includes M. tuberculosis, M. africanum, M. canneti, M. microti, and M. bovis. The members of the
complex are also known by slow growing nature with doubling time ranging from 12 to 24 hours which of course affected by pathogen character and environmental factors. Despite the genotypic similarity amongst the members of MTBC, they differ greatly in terms of their ability to cause disease, host preferences, and phenotypic characteristics.”

- Page 4, paragraph 8 and 9 are paraphrased as: “Molecular typing of M. tuberculosis is applied to study the type of strain circulating, distinguishing relapse strain versus re-infection, or detecting laboratory cross-contamination of M. tuberculosis strain and overall evaluating the TB control programmes. With this aim, the currently available M. tuberculosis genotyping tools are not equally appropriate. For instance, restriction fragment length polymorphism (RFLP) analysis which bases on the monitoring the number of insertion sequence IS6110 in the chromosome which varies among different strains and mycobacterial interspersed repetitive units-variable tandem repeats of DNA tandem repeats (MIRU-VNTRs) which rely on measuring repetitive DNA elements are tools known by having relatively highly discriminatory power compared to spoligotyping that detects polymorphisms present in a direct repeat (DR) locus. Although spoligotyping is also prone to homoplasy as individual spacers can be deleted independently in phylogenetically unrelated strains, it has several large international databases that compiled thousands of clinical isolates from many countries.”

2. Result section, Page 7, under Spoligotyping results of M. tuberculosis strains from Ethiopia sub section, line 2 …. (Table 1) is added.

3. Titles of Figures are removed from files of Figure 1, Figure 2, Figure 3, and figure 4.